miR-34/449 miRNAs are required for motile ciliogenesis by repressing cp110.

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Public Summary:
Here we show that members of the microRNA family miR34-449 help to control assembly of motile cilia, organelles that are responsible for cell motility and extracellular fluid movement. Mice deficient for all members of the miR34-449 family have shortened lifespan and reproductive and respiratory dysfunction due to defective motile cilia. In both mouse and Xenopus, miR-34/449-deficient multiciliated cells exhibit a significant decrease in cilia length and number. Our data show that miR-34/449 promote ciliogenesis by down regulating Cp110, a protein that itself inhibits the assembly of cilia. Altogether, our findings elucidate conserved cellular and molecular mechanisms through which miR-34/449 regulate motile ciliogenesis.

Scientific Abstract:
The mir-34/449 family consists of six homologous miRNAs at three genomic loci. Redundancy of miR-34/449 miRNAs and their dominant expression in multiciliated epithelia suggest a functional significance in ciliogenesis. Here we report that mice deficient for all miR-34/449 miRNAs exhibited postnatal mortality, infertility and strong respiratory dysfunction caused by defective mucociliary clearance. In both mouse and Xenopus, miR-34/449-deficient multiciliated cells (MCCs) exhibited a significant decrease in cilia length and number, due to defective basal body maturation and apical docking. The effect of miR-34/449 on ciliogenesis was mediated, at least in part, by post-transcriptional repression of Cp110, a centriolar protein suppressing cilia assembly. Consistent with this, cp110 knockdown in miR-34/449-deficient MCCs restored ciliogenesis by rescuing basal body maturation and docking. Altogether, our findings elucidate conserved cellular and molecular mechanisms through which miR-34/449 regulate motile ciliogenesis.